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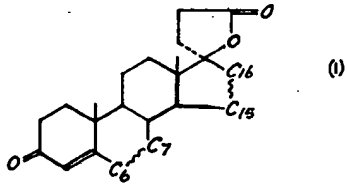
(19)

(54) NEW STEROID SPIROLACTONES AND PROCESS FOR THEIR PREPARATION

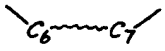
(71) We, SCHERING AKTIENGESELLSCHAFT, a body corporate organised according to the laws of the Federal Republic of Germany, of Berlin and Bergkamen, Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention provides, as new compounds, spirolactones of the general formula (I)

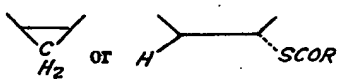


(I)

in which

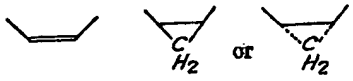


stands for the grouping



where R represents a lower alkyl radical having up to 5 carbon atoms, and

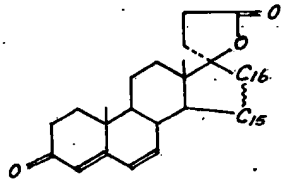
stands for the grouping



As lower alkyl radicals there may be mentioned, more especially, methyl, ethyl and n-propyl radicals.

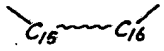
The compounds according to the invention have valuable pharmacological properties. They are, among other things, diuretic agents of the aldosterone antagonist type, i.e. they reverse the action of desoxycorticosterone to sodium and potassium excretion. In Hollmann's test method (G. Hollmann et. al., Tubuläre Wirkungen und renale Elimination von Spirolactones, Naunyn-Schmeidebergs Arch. Exp. Path. Pharmak. *247* (1964) 419; P Marx, Renale Wirkungen des d-Aldosterone und seines Antagonisten Spironolactons, Diss. Med. Fak. FU Berlin 1966) the action of the compounds according to the invention proves, surprisingly, to be superior to that of the known spironolactone.

The invention further provides a process for the production of spirolactones of the general formula I, wherein a Δ^6-unsaturated spirolactone of the general formula (II)



(II)

in which



has the meaning given above, is methylenated or thioacylated in a manner known *per se*.

The methylenation of the compounds according to formula (II) is effected according to methods known *per se*, for example by reaction with dimethyl sulphoxonium methylide in an aprotic solvent such, for example, as dimethyl sulphoxide, dimethylformamide, dioxan or a mixture or dimethyl sulphoxide and tetrahydrofuran, the operation being effected, advantageously, at 20—40°C under an inert gas such, for example, as nitrogen.

The dimethyl sulphoxonium methylide is advantageously produced from trimethyl sulphoxonium iodide or chloride with a base such, for example, as sodium hydride, sodium

hydroxide, potassium tertiary butylate or sodium methylate.

The compounds according to formula (II) are thioacylated likewise according to methods known *per se*. Particularly suitable is the reaction with the corresponding thio-acid in the presence of a protic solvent such, for example, as methanol and ethanol, also in admixture with water, under heat, in particular in the temperature range of above room temperature up to the boiling temperature of the reaction mixture.

It is, however, also possible to effect thioacylation without a solvent.

The starting material 3 - oxo - 4,6,15 - androstatriene - [17 - (β - 1') - spiro - 5'] perhydrofuran - 2' - one may be produced as follows:

4.34 g of freshly compressed lithium are added to 20.0 g of 3β - hydroxy - 5,15 - androstadien - 17 - one in 280 ml of absolute tetrahydrofuran. Then, while cooling with ice, 36 ml of 1 - bromo - 3 - dimethoxypropane are added dropwise within 30 minutes. After stirring for 1.5 hours at the temperature of the ice bath, the unreacted lithium is filtered off and the filtrate is stirred into ice water. The precipitate is filtered off, washed with water and taken up in methylene chloride.

After drying and evaporating, the residue is chromatographed on silica gel. 19.9 g of 17α - (3' - dimethoxypropyl) - 5,15 - androstadiene - 3β,17β - diol are obtained in the form of an oil.

1.0 g of *p*-toluenesuphonic acid are added, while cooling with ice, to 19.9 g of 17α - (3' - dimethoxypropyl) - 5,15 - androstadiene - 3β,17β - diol in 500 ml of acetone and stirring is effected for 15 minutes while cooling. The mixture is then stirred into ice water containing sodium hydrogen carbonate, the precipitate is filtered off, washed and taken up in methylene chloride. After drying and evaporating, 19.2 g of crude 2'ξ - methoxy - 3β - hydroxy - 5,15 - androstadiene - [17(β - 1') - spiro - 5'] - perhydrofuran are obtained in the form of an oil.

3.94 g of aluminium isopropylate in 40 ml of toluene are added to 19.2 g of 2'ξ - methoxy - 3β - hydroxy - 5,15 - androstadiene - [17(β - 1') - spiro - 5'] perhydrofuran in 394 ml of absolute toluene and 39.4 ml of cyclohexanone and heated for 45 minutes while distilling off slowly. The mixture is then diluted with methylene chloride, washed with dilute sulphuric acid and water, dried and evaporated. The residue is chromatographed on silica gel. 17.5 g of 2'ξ - methoxy - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] perhydrofuran are obtained in the form of an oil.

UV: ε_{289} = 16200.

35 ml of chromosulphuric acid (produced from 267 g of CrO_3, 400 ml of water and 230 ml of concentrated sulphuric acid, made up to 1 litre with water) are added, while cooling with ice, to 17.5 g of 2'ξ - methoxy - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] - perhydrofuran in 350 ml of acetone and the whole is stirred for 30 minutes while cooling with an ice bath. The whole is then stirred into ice water, the precipitate is filtered off, washed with water and taken up in methylene chloride. After drying and evaporating, the residue is chromatographed on silica gel. 11.8 g of 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] perhydrofuran - 2' - one are obtained. A sample recrystallised from diisopropyl ether/acetone melts at 189.5—191.5°C.

UV: ε_{240} = 17,300.

10 ml of orthoformic acid triethyl ester and 10 ml of dioxan/concentrated sulphuric acid (produced from 13.5 ml of absolute dioxan and 0.48 ml of concentrated sulphuric acid) are added to 10.0 g of 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] - perhydrofuran - 2' - one in 100 ml of absolute dioxan. Stirring is effected for 30 minutes at room temperature, 2 ml of pyridine are added and dilution is effected with ether. The ether phase is washed with water, dried and evaporated. The residue is triturated with methanol containing pyridine and the separated crystals are suction-filtered. 8.9 g of 3 - ethoxy - 3,5,15 - androstatriene - [17(β - 1') - spiro - 5'] perhydrofuran - 2' - one with a melting point of 153.5—159°C are obtained.

UV: ε_{240} = 19,800.

8.9 g of 3 - ethoxy - 3,5,15 - androstatriene - [17(β - 1') - spiro - 5'] perhydrofuran - 2' - one are dissolved in 201 ml of acetone, cooled in an ice bath and 1.38 ml of pyridine, 6.36 g of sodium acetate and 63.6 ml of water are added. 4.72 g of N - bromosuccinimide are then added and 6.36 ml of acetic acid are added dropwise in the course of 15 minutes. Stirring is effected for 45 minutes while cooling with ice, dilution is effected with ether and the whole is washed neutral with water. After drying and evaporating, 10.35 g of 6β - bromo - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] perhydrofuran - 2' - one are obtained in the form of an oil.

UV: ε_{243} = 12,700.

10.35 g of 6β - bromo - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5'] perhydrofuran - 2' - one in 103.5 ml of dimethylformamide are stirred with 4.67 g of lithium carbonate and 5.37 g of lithium bromide for 18 hours at 100°C. The whole is then stirred into ice water, the precipitate is filtered off, washed with water and taken up in methylene chloride. After drying and evaporating, the residue is chromatographed. After recrystallising from diisopropyl ether/acetone 6.5 g of 3 - oxo - 4,6,15 - androstatriene - [17(β - 1') - spiro - 5'] perhydro-

furan - 2' - one with a melting point of 182.5—184.5°C are obtained.

UV: ε_{284}=27,100.

The starting material, 15α,16α - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one, may be produced in the following manner:

3.6 g of lithium are added, while cooling with ice, to 15 g of 3β - hydroxy - 15α,16α - methylene - 5 - androsten - 17 - one (produced, for example, according to German Offenlegungsschrift 2,109,555) in 150 ml of absolute tetrahydrofuran and then 30 ml of 1 - bromo - 3 - dimethoxypropane are added dropwise in the course of 30 minutes. After stirring for 2.5 hours at ice bath temperature the unreacted lithium is separated and the filtrate is stirred into ice water. The resulting precipitate is filtered off, washed with water and taken up in methylene chloride. After drying and evaporating, the residue is chromatographed on silica gel. 16.8 g of 17α - (3' - dimethoxypropyl) - 15α,16α - methylene - 5 - androstene - 3β,17β - diol are obtained. A sample recrystallised from diisopropyl ether/acetone melts at 153—159°C.

16.5 g of 17α - (3' - dimethoxypropyl) - 15α,16α - methylene - 5 - androstene 3β,17β - diol are stirred in 410 ml of 70% acetic acid for 18 hours at room temperature. The whole is stirred into ice water, the resulting precipitate is filtered off, taken up in chloroform and washed with sodium hydrogen carbonate solution and water. After drying and evaporating, the residue is chromatographed on silica gel. 11.5 g of 3β - hydroxy - 15α,16α - methylene - 5 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2'ξ - ol are obtained. A sample recrystallised from diisopropyl ether/acetone melts at 194—202°C.

21 ml of cyclohexanone and 2.1 g of aluminium isopropylate in 20 ml of absolute toluene are added to 10.5 g of 3β - hydroxy - 15α,16α - methylene - 5 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2'ξ - ol in 210 ml of absolute toluene and heated for 45 minutes while distilling off slowly. The whole is then diluted with methylene chloride, washed with 2N sulphuric acid and water, dried and evaporated. 11.5 g of crude 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - ol are obtained in the form of an oil. A sample purified by means of preparative layer chromatography and recrystallisation from diisopropyl ether/acetone melts at 259—268°C.

UV: ε_{241}=16,500.

10 ml of chromosulphuric acid (produced from 267 g of CrO_3, 400 ml of water and 230 ml of concentrated sulphuric acid, then made up to 1 litre with water) are added, while cooling with ice, to 10.5 g of 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2'ξ - ol in 100 ml of acetone and the whole is stirred for one hour. The mixture is stirred into ice water, washed with water and taken up in methylene chloride. After drying and evaporating, the residue is chromatographed on silica gel, 8.2 g of 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained. A sample recrystallised from diisopropyl ether/acetone melts at 180—181°C.

UV: ε_{240}=16,600.

A solution of 7.2 ml of absolute dioxan and 0.26 ml of concentrated sulphuric acid are added to 7.2 g of 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 72 ml of absolute dioxan and 7.2 ml of orthoformic acid triethyl ester and stirred for 30 minutes at room temperature. 2 ml of pyridine are then added, the whole is diluted with ether, washed with water and dried. After evaporation 8.5 g of crude 3 - ethoxy - 15α,16α - methylene - 3,5 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

UV: ε_{241}=15,700.

8.5 g of 3 - ethoxy - 15α,16α - methylene - 3,5 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are dissolved in 192 ml of acetone, cooled in an ice bath and then 1.32 ml of pyridine, 6.08 g of sodium acetate and 60.8 ml of water are added followed by 4.51 g of N - bromosuccinimide and then 6.08 ml of acetic acid are added dropwise in the course of 10 minutes. The whole is stirred for one hour at ice bath temperature, diluted with ether, washed with water and dried. After evaporating, 9.6 g of crude 15α,16α - methylene - 6β - bromo - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

9.6 g of 15α,16α - methylene - 6β - bromo - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 96 ml of dimethylformamide are stirred for 18 hours at 100°C with 3.75 g of lithium carbonate and 4.4 g of lithium bromide. The whole is then stirred into ice water, the resulting precipitate is filtered off, taken up in methylene chloride, washed with 2N sulphuric acid and water and dried. After evaporating, the residue is chromatographed on silica gel. 6.5 g of 15α,16α - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained. A sample recrystallised from diisopropyl ether melts at 180.5—182.5°C.

UV: ε_{288}=26,300.

The starting material, 15β,16β - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spir - 5']perhydrofuran - 2' - one may be produced in the following manner:

15 g of 3β - hydroxy - 15β,16β - methylene - 5 - androsten - 17 - one (produced, for example, according to German Patent Specification 1,593,500) in 150 ml of absolute tetrahydrofuran are reacted for 2 hours at ice bath temperature and 4 hours at room temperature with 3.27 g of lithium and 29 ml of 1 - bromo - 3 - dimethoxypropane. The unreacted lithium is separated by filtration, the filtrate is stirred into ice water, the precipitate is filtered off and taken up in methylene chloride. After drying and evaporating, the residue is chromatographed on silica gel. 17.4 g of 17α - (3' - dimethoxypropyl) - 15β,16β - methylene - 5 - androstene - 3β,17β - diol are obtained.

17.0 g of 17α - (3' - dimethoxypropyl) - 15β,16β - methylene - 5 - androstene - 3β,17β - diol are stirred in 340 ml of 70% acetic acid for 18 hours at room temperature. The whole is stirred into ice water, the resulting precipitate is filtered off and taken up in methylene chloride. The methylene chloride phase is washed with sodium hydrogen carbonate solution and water, dried and evaporated. 13.8 g of 3β - hydroxy - 15β,16β - methylene - 5 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - ol are obtained as a crude product.

1.76 g of aluminium isopropylate in 50 ml of absolute toluene are added to 8.8 g of 3β - hydroxy - 15β,16β - methylene - 5 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2'ξ - ol in 176 ml of absolute toluene and 17.6 ml of cyclohexanone and heated for 3 hours while distilling off slowly. The whole is then diluted with ether, washed with 2N sulphuric acid and water, dried and evaporated. The residue is chromatographed on silica gel. 4.3 g of 15β,16β - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained. A sample recrystallised from diisopropyl ether/acetone melts at 178.5—179.5°C.

UV: ε_{241}=16,500.

4.2 g of 15β,16β - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5')perhydrofuran - 2' - one in 84 ml of tertiary butanol are heated for 18 hours under reflux with 4.2 g of chloranil. The solvent is distilled off *in vacuo* and the residue is chromatographed on silica gel. Preparative layer chromatography is used for further purification. 1.1 g of 15β,16β - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained in the form of an oil.

UV: ε_{284}=25,700.

After the reaction is complete the reaction mixture is worked up in a conventional manner, such as by precipitation, extraction, recrystallisation and/or chromatography.

The pharmacologically active compounds according to the invention of the general formula (I) can be made up, according to methods of galenical pharmacy known *per se*, in the form of pharmaceutical preparations. Accordingly, the invention also provides a pharmaceutical preparation which comprises a compound of the general formula (I) in admixture or conjunction with a pharmaceutically suitable carrier. The preparations are more especially in a form suitable for oral administration, especially tablets.

Advantageously the preparations are made up in dosage unit form, and each dosage unit preferably contains from 10 to 100 mg of the active ingredient. The dosage of the compound according to the invention in the case of human beings may be 20—500 mg/day.

The following Examples illustrate the invention:

Example 1

1.5 g of 3 - oxo - 4,6,15 - androstatriene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 22.5 ml of methanol are heated for 2 hours under reflux with 1.5 ml of thioacetic acid. The whole is then diluted with ether, washed with water, sodium hydrogen carbonate solution and water, dried and evaporated. The residue is chromatographed on silica gel. 1.05 g of 7α - acetylthio - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one having a melting point of 317—319°C (decomposition) are obtained.

UV: ε_{238}=19,800.

Example 2

1.0 g of 3 - oxo - 4,6,15 - androstatriene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 15 ml of methanol is heated under reflux for 16 hours with 1 ml of thiopropionic acid. The whole is worked up as described in Example 1 and purified. 670 mg of 3 - oxo - 7α - propionylthio - 4,15 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

UV: ε_{238}=18,500.

Example 3

4.13 g of trimethylsulphoxonium iodide in 75 ml of dimethyl sulphoxide are stirred for 2 hours under nitrogen with 512 mg of an 80% sodium hydride oil suspension. 3.0 g of 3 - oxo - 4,6,15 - androstatriene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are added to the almost clear solution and stirred for 24 hours at room temperature. The whole is then stirred into ice water, the precipitate is filtered off, washed with water and taken up in ether. After drying and evaporating, the residue is chromatographed on silica gel and then further purified by means of preparative layer chromatography. 520 mg of 6β,7β - methylene - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

UV: ε_{266}=18,100.

Example 4

1.4 g of 15α,16α - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 22.5 ml of methanol are heated under reflux for 17 hours with 3 ml of thioacetic acid. The whole is then diluted with ether, washed with sodium hydrogen carbonate solution and water, dried and evaporated. The residue is purified by means of preparative layer chromatography and recrystallised from diisopropyl ether/acetone. 1.08 g of 7α - acetylthio - 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one with a melting point of 214.5—217.5°C are obtained.

UV: ε_{238} = 19,100.

Example 5

500 mg of 15α,16α - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 5 ml of methanol are heated under reflux for 32 hours with 1 ml of thiopropionic acid. The whole is worked up and purified as described in Example 4. 220 mg of 15α,16α - methylene - 3 - oxo - 7α - propionylthio - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

UV: ε_{238} = 18,700.

Example 6

2.75 g of trimethylsulphoxonium iodide in 57 ml of dimethyl sulphoxide are stirred with 341 mg of an 80% sodium hydride oil suspension for 2 hours at room temperature. 2.0 g of 15α,16α - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are added, under nitrogen, to the almost clear solution and stirred for 24 hours at room temperature. The whole is then stirred into ice water, the resulting precipitate is filtered off, washed with water, and taken up in methylene chloride. After drying and evaporating, the residue is purified by subjecting it to preparative layer chromatography several times. 520 mg of 6β,7β,15α,16α - dimethylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained.

UV: ε_{206} = 18,000.

Example 7

1.0 g of 15β,16β - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 15 ml of methanol is heated under reflux for 2 hours with 1 ml of thioacetic acid. The whole is then taken up in ether, washed with sodium hydrogen carbonate solution and water, dried and evaporated. The residue is chromatographed on silica gel. Recrystallisation is effected from diisopropyl ether/acetone and 590 mg of 7α - acetylthio - 15β,16β - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained with a melting point of 242—247°C (decomposition).

UV: ε_{238} = 19,300.

Example 8

750 mg of 15β,16β methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one in 7.5 ml of methanol are heated under reflux for 18 hours with 0.75 ml of thiopropionic acid. The whole is worked up as described in Example 4 and the residue is purified by means of preparative layer chromatography. 320 mg of 15β,16β - methylene - 3 - oxo - 7α - propionylthio - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained in the form of an oil.

UV: ε_{238} = 18,700.

Example 9

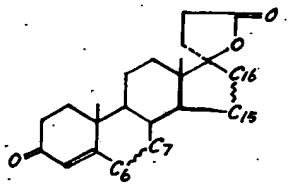
1.4 g of trimethylsulphoxonium iodide in 25 ml of dimethyl sulphoxide are stirred under nitrogen for 1.5 hours with 170 mg of an 80% sodium hydride oil suspension. 1.0 g of 15β,16β - methylene - 3 - oxo - 4,6 - androstadiene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one, dissolved in 10 ml of dimethyl sulphoxide, is added to the almost clear solution. After stirring for 24 hours at room temperature the whole is stirred into ice water, the resulting precipitate is filtered off, taken up in ether, washed with water and dried. The residue obtained after evaporating is purified by subjecting it several times to preparative layer chromatography. 170 mg of 6β,7β,15β,16β - dimethylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one are obtained in the form of an oil.

UV: ε_{206} = 18,400.

WHAT WE CLAIM IS:—

1. A spirolactone of the general formula

(I)



(I)

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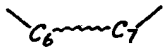

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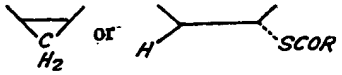
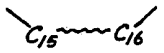
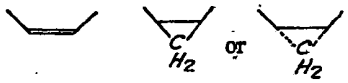


where R represents a lower alkyl radical having up to 5 carbon atoms and



stands for the grouping



2. 7α - Acetylthio - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5']-perhydrofuran - 2' - one.

3. 3 - Oxo - 7α - propionylthio - 4,15 - androstadiene - [17(β - 1') - spiro - 5']-perhydrofuran - 2' - one.

4. 6β,7β - Methylene - 3 - oxo - 4,15 - androstadiene - [17(β - 1') - spiro - 5']-perhydrofuran - 2' - one.

5. 15α,16α - Methylene - 3 - oxo - 7α - propionylthio - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

6. 6β,7β,15α,16α - Dimethylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

7. 7α - Acetylthio - 15α,16α - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

8. 7α - Acetylthio - 15β,16β - methylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

9. 15β,16β - Methylene - 3 - oxo - 7α - propionylthio - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

10. 6β,7β,15β,16β - Dimethylene - 3 - oxo - 4 - androstene - [17(β - 1') - spiro - 5']perhydrofuran - 2' - one.

11. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 1 to 10, in admixture or conjunction with a pharmaceutically suitable carrier.

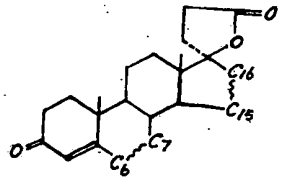
12. A pharmaceutical preparation as claimed in claim 11, which is in a form suitable for oral administration.

13. A pharmaceutical preparation as claimed in claim 11 or 12, which is in dosage unit form.

14. A pharmaceutical preparation as claimed in claim 12 or 13, which is in the form of a tablet.

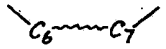
15. A pharmaceutical preparation as claimed in any one of claims 12 to 14, which contains from 10 to 100 mg of the active ingredient per dosage unit.

16. A process for the manufacture of spirolactones of the general formula (I)

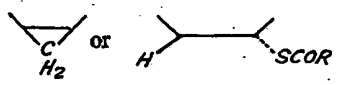


(I)

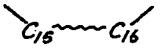
in which



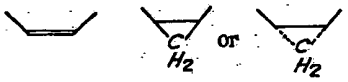
stands for the grouping



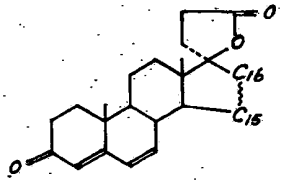
where R represents a lower alkyl radical having up to 5 carbon atoms, and



stands for the grouping

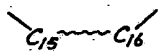


wherein a Δ^6-unsaturated spirolactone of the general formula (II)



(II)

in which



has the meaning given above, is methylenated or thioacylated in a manner known *per se*.

17. A process as claimed in claim 16, conducted substantially as described in any one of Examples 1 to 9.

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